IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BOEHRINGER INGELHEIM PHARMACEUTICALS INC., BOEHRINGER INGELHEIM INTERNATIONAL GMBH, BOEHRINGER INGELHEIM CORPORATION and BOEHRINGER INGELHEIM PHARMA GMBH & CO. KG, Plaintiffs, v. APOTEX INC. and APOTEX CORP. Defendants.	C.A. No. 23-cv-0685-CFC **ANDA CASE** [redacted] **ORAL ARGUMENT REQUESTED** **REDACTED - PUBLIC VERSION**

REPLY BRIEF IN SUPPORT OF
APOTEX'S MOTION FOR JUDGMENT ON THE PLEADINGS

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

Other Authorities

I. SUMMARY OF ARGUMENT.

BI takes a shotgun approach in its opposition brief (D.I. 35), but its concessions are dispositive. BI concedes:

(i) Apotex does not directly infringe;

(ii) Apotex carved out from its label the only clinical trial focused on patients with *severe* renal impairment;

(iii) Apotex's Product will be indicated for patients *regardless of their eligibility for metformin*;

(iv) Apotex's Label instructs that Apotex's Product be used in patients *eligible* for metformin; and

(v) there are noninfringing uses.

BI thus retreats to arguing that text in Apotex's Label regarding patients with "renal impairment" will lead to "inevitable" infringement by physicians. This is wrong. First, "renal impairment" is not synonymous with "ineligible for metformin." But even if it were (it's not), BI does not identify anything in Apotex's Label that can plausibly be construed as a specific recommendation—much less instruction—to use Apotex's Product in patients ineligible for metformin. BI's inducement claim is not plausible under any plain reading of Apotex's Label, which controls here. BI's contributory infringement theory is equally meritless given the admittedly noninfringing use of treating patients

eligible for metformin, which is substantial by any measure; BI cannot credibly claim otherwise.

Judgment of noninfringement is warranted.

II. ARGUMENT.

A. RULE 12(C) IS USED TO DISPOSE OF HATCH-WAXMAN CLAIMS.

BI complains that this Rule 12(c) motion precludes fact discovery. But fact discovery is unnecessary, and judgment on the pleadings is appropriate, because Apotex's Label shows noninfringement and there are no material issues of fact. *See* Apotex Op. Brief (D.I. 27) at § IV.B.1.

B. BI'S INDUCED INFRINGEMENT CLAIM FAILS.

BI's claim for induced infringement fails because it is not plausible. BI does not dispute key facts, and does not identify any promotion—much less instruction—in Apotex's Label regarding the use of Apotex's Product in patients ineligible for metformin. Instead, BI points to "renal impairment" language and wrongly equates that with "ineligible for metformin." Further, the scant text in Apotex's Label pertaining to patients with *severe* renal impairment at most describes a potentially infringing use.

1. BI Does Not Dispute Key Facts.

BI does not (and cannot) dispute the key facts requiring judgment for Apotex:

- [redacted]
- Apotex's Product will be indicated to treat patients *regardless of eligibility for metformin*; and
- [redacted]

See D.I. 27 at 7-10; 15.

2. "Renal Impairment" Does Not Mean "Ineligible for Metformin," and Apotex's Label Merely Allows Apotex's Product to Be Used in Various Patient Populations.

Because it cannot dispute these facts, BI hinges its inducement theory on text in Apotex's Label concerning "renal impairment." This fails on multiple levels.

First, "renal impairment" does not mean "ineligible for metformin." Second, the little text in Apotex's Label pertaining to patients with *severe* renal impairment (who may be ineligible for metformin) only shows that Apotex's Label allows for use in all patient populations, and does not instruct use in the claimed population. This is confirmed by the documents *BI* uses in support: the shared written description of the patents-in-suit and the Glucophage Label. Indeed, the more

closely BI's citations are examined, the more apparent it is that Apotex's Label does not promote—much less instruct—the use of Apotex's Product in patients ineligible for metformin.

a. Shared Written Description and the Glucophage Label.

BI's reliance on the written description and the Glucophage Label is wholly misplaced because these documents confirm noninfringement.[1]

The written description defines renal impairment, explaining that there are five stages, with stages 1-3 having glomerular filtration rates ("GFRs") of ≥ 30 ml/min/1.73 m^2, and stages 4-5 having GFRs of ≤ 30 ml/min/1.73 m^2. Stage 4 constitutes "severe renal impairment" and stage 5 is "end-stage renal disease":

> For other more detailed example, patients with renal disease, renal dysfunction or renal impairment include patients with chronic renal insufficiency or impairment, which can be stratified according to glomerular filtration rate (GFR, ml/min/1.73 m^2) into 5 disease stages: stage 1 characterized by normal GFR ≥90 plus either persistent albuminuria or known structural or hereditary renal disease; stage 2 characterized by mild reduction of GFR (GFR 60-89) describing mild renal impairment; stage 3 characterized by moderate reduction of GFR (GFR 30-59) describing moderate renal impairment; stage 4 characterized by severe reduction of GFR (GFR 15-30) describing severe renal impairment; and terminal stage 5 characterized by requiring dialysis or GFR <15 describing established kidney failure (end-stage renal disease, ESRD).

[1] Thus, BI's argument that the Court must credit allegations about "scientific" facts as true (D.I. 35 at 10) favors Apotex, not BI.

877 Patent, D.I. 2 Ex. 2 at 3:35-49.[2] Thus, for a patient to have severe renal impairment, the patient must have a GFR ≤ 30 ml/min/1.73 m^2.

Consistent with the written description, the Glucophage Label teaches Glucophage should not be used in patients with a GFR below 30 ml/min/1.73 m^2:

- Do not use in patients with eGFR below 30 mL/minute/1.73 m^2 (2.3)
- Initiation is not recommended in patients with eGFR between 30-45 mL/minute/1.73 m^2 (2.3)
- Assess risk/benefit of continuing if eGFR falls below 45 mL/minute/1.73 m^2 (2.3)
- Discontinue if eGFR falls below 30 mL/minute/1.73 m^2 (2.3)

D.I. 25 Ex. 1 at 1. In sum, only "severe renal impairment" patients might be ineligible for metformin.

b. BI's Label Citations.

Despite these undisputed facts, BI equates "renal impairment" with "ineligible for metformin" and focuses on portions of Apotex's label concerning "renal impairment." Indeed, BI affirmatively mischaracterizes the written description and the Glucophage Label, arguing "Apotex's Label goes far beyond merely describing an infringing mode. It provides dosage instructions for administering linagliptin to *renally impaired patients (who are, by definition, ineligible for metformin)*…."). D.I. 35 at 16.

BI also cobbles together citations from different studies and cites the same passages in Apotex's Label multiple times in a transparent attempt to inflate their

[2] All emphasis added.

volume and import. For example, BI argues that [redacted] and then cherry-picks certain isolated phrases from pages 8, 10, and 17 of Apotex's Label. D.I. 35 pp. 13-14. *See also id*. at 7, 8, 14, 16 (same citations).

Apotex parses out these confusing citations below.

[redacted]

D.I. 27 Ex. C at 6.

[redacted]

[3] [redacted]

D.I. 27, Ex. C at 17. Thus, there is nothing about CARMELINA that specifically promotes the use of Apotex's Product in patients ineligible for metformin.

[redacted]

Id. at 8. Thus, there is nothing about the PK study that specifically promotes the use of Apotex's Product in patients ineligible for metformin.

[redacted]

[redacted]

Id. at 10. [redacted]

3. BI's Caselaw Discussion Fails to Address, Much Less Apply, What Constitutes Necessary Promotion.

BI also fails to meaningfully distinguish Apotex's cases, and omits any analysis comparing the law to the instant facts.

Takeda sets forth the proper analysis for inducement:

> *[I]nstructions need to evidence intent to encourage infringement*. *The question is not just whether instructions describe the infringing mode, but whether the instructions teach an infringing use* of the device such that we are willing to infer from those instructions an affirmative intent to infringe the patent. *Merely describing an infringing mode is not the same as* recommending, encouraging or promoting an infringing use, or *suggesting that an infringing use should be performed*.

Takeda Pharms. U.S.A., Inc. v. West-Ward Pharm. Corp., 785 F.3d 625, 631 (Fed. Cir. 2015) (all quotations, marks, and citations omitted).

Further, given that the "[Hatch-Waxman] statute was designed to enable the sale of drugs for non-patented uses," "*vague label language cannot be combined with speculation* about how physicians may act to find inducement." *Id.* at 631-632.

4. Under a Proper Interpretation of the Caselaw, It Is Implausible that Apotex's Label Induces Infringement.

Here, BI must set forth a plausible claim that Apotex's Label actually teaches that Apotex's Product should be administered to patients ineligible for metformin. BI does not and cannot do so on this record.

As discussed, Apotex's Product will be indicated to treat patients regardless of eligibility for metformin, and Apotex's Label is full of instruction and encouragement to use Apotex's Product in patients eligible for metformin. *See* D.I. 27 at 8-10.

[redacted] Thus—contrary to BI's arguments—*Genentech*, *HZNP Meds*., and *Amarin* are all directly on point. *See Genentech, Inc. v. Sandoz, Inc*., 592 F. Supp. 3d 355, 368 (D. Del. 2022) (a label "merely provid[ing] physicians with multiple…options, some covered by the Asserted Patents and some not, and leaves [the choice of options] to the physician's clinical judgment" does not evince specific intent); *HZNP Meds. LLC v. Actavis Lab'ys UT, In*c., 940 F.3d 680, 702 (Fed. Cir. 2019) (no intent to induce where label's instructions were broader than claimed method, and did not require users to perform claimed method); *Amarin Pharma, Inc. v. Hikma Pharms. USA Inc*., 578 F. Supp. 3d 642, 647 (D. Del. 2022) (Andrews, J.) (granting generic's motion to dismiss: "[T]he broader category [included in the label] simply includes both infringing and non-infringing uses, without 'specifically encourag[ing]' the use of the generic for the non-infringing uses….").

Nor is this phrase an instruction (or recommendation) to infringe—therefore, BI's arguments and cases regarding "inevitable" infringement (D.I. 35 at 2-3, 11,

19) are inapposite because a specific recommendation/instruction is necessary for "inevitable" infringement.[4]

BI's claim for induced infringement is implausible and must fail.

C. BI'S CONTRIBUTORY INFRINGEMENT CLAIM FAILS.

As for contributory infringement, BI does not dispute that Apotex's Product is suitable for the noninfringing use of treating patients eligible for metformin, which is all over the Apotex Label. Instead, BI argues that whether the use is substantial is "an intensely factual inquiry not suitable for determination at the pleadings stage." D.I. 35 at 21.

Respectfully, this is nonsensical given that "a substantial non-infringing use is any use that is 'not unusual, far-fetched, illusory, impractical, occasional, aberrant, or experimental.'" *In re Bill of Lading*, 681 F.3d 1323, 1377 (Fed. Cir. 2012) (quotation omitted).

[4] *See Eli Lilly & Co. v. Teva Parenteral Meds., Inc.*, 845 F.3d 1357, 1369 (Fed. Cir. 2017) (label included "repeated instructions"); *Vanda Pharms. Inc. v. West-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117, 1132 (Fed. Cir. 2018) (patent required genotyping; court found label recommended genotyping); *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010) (patents required once-daily dosing; label specifically instructed to titrate down to the lowest effective dose, which was once-daily); *Sanofi v. Glenmark Pharms. Inc., USA*, 204 F. Supp. 3d 665, 673-74, 679-80 (D. Del. 2016) (finding "clear encouragement of the [claimed] use").

Here, it is undisputed that: (i) Apotex's Product will be indicated for use regardless of a patient's eligibility for metformin; and (ii) Apotex's Label repeatedly says Apotex's Product can be taken with metformin.

Therefore, it strains credulity to suggest that using Apotex's Product in patients eligible for metformin is not a "substantial" noninfringing use.

III. CONCLUSION.

Apotex respectfully requests the Court enter judgment of noninfringement under Rule 12(c).

Dated: January 26, 2024

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CERTIFICATE OF SERVICE

I, Megan C. Haney, Esquire, hereby certify that, on January 26, 2024, a copy of REPLY BRIEF IN SUPPORT OF APOTEX'S MOTION FOR JUDGMENT ON THE PLEADINGS was served on the following counsel via the manner indicated:

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